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In re Application of

Samuel Weiss

Application Number

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US005851832A

## United States Patent [19]

Weiss et al.

[11] Patent Number: 5,851,832  
 [45] Date of Patent: Dec. 22, 1998

## [54] IN VITRO GROWTH AND PROLIFERATION OF MULTIPOTENT NEURAL STEM CELLS AND THEIR PROGENY

[75] Inventors: Samuel Weiss; Brent Reynolds, both of Alberta, Canada; Joseph P. Hammang; E. Edward Baetge, both of Barrington, R.I.

[73] Assignee: Neurospheres, Ltd., Canada

[21] Appl. No.: 486,648

[22] Filed: Jun. 7, 1995

## Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 270,412, Jul. 5, 1994, abandoned, which is a continuation of Ser. No. 726,812, Jul. 8, 1991, abandoned, and a continuation-in-part of Ser. No. 385,404, Feb. 7, 1995, abandoned, which is a continuation of Ser. No. 961,813, Oct. 16, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 359,945, Dec. 20, 1994, abandoned, which is a continuation of Ser. No. 221,655, Apr. 1, 1994, abandoned, which is a continuation of Ser. No. 967,622, Oct. 28, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, and Ser. No. 376,062, Jan. 20, 1995, abandoned, which is a continuation of Ser. No. 10,829, Jan. 29, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 149,508, Nov. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 311,099, Sep. 23, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812, and Ser. No. 338,730, Nov. 14, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812.

[51] Int. Cl. 6 C12N 5/06; C12N 5/08; C12N 5/02  
 [52] U.S. Cl. 435/368; 435/325; 435/366; 435/383; 435/384  
 [58] Field of Search 435/240.2, 325, 435/366, 368, 377, 383, 384

## [56] References Cited

## U.S. PATENT DOCUMENTS

|           |         |               |           |
|-----------|---------|---------------|-----------|
| 4,753,635 | 6/1988  | Sagen et al.  | 604/49    |
| 4,980,174 | 12/1990 | Sagen et al.  | 424/563   |
| 5,082,670 | 1/1992  | Gage          | 424/520   |
| 5,175,103 | 12/1992 | Lee et al.    | 435/172.3 |
| 5,411,883 | 5/1995  | Boss et al.   | 435/29    |
| 5,612,211 | 3/1997  | Wilson et al. | 435/378   |

## FOREIGN PATENT DOCUMENTS

|           |         |                    |
|-----------|---------|--------------------|
| 0 233 838 | 8/1987  | European Pat. Off. |
| 89/03872  | 5/1989  | WIPO               |
| 90/06757  | 6/1990  | WIPO               |
| 91/02003  | 2/1991  | WIPO               |
| 91/09936  | 7/1991  | WIPO               |
| 91/17242  | 11/1991 | WIPO               |
| 93/01275  | 1/1993  | WIPO               |
| 93/09802  | 5/1993  | WIPO               |
| 94/03199  | 2/1994  | WIPO               |

## OTHER PUBLICATIONS

Almazan et al., "Epidermal Growth and Bovine Growth Hormone Stimulate Differentiation and Myelination of Brain Cell Aggregates in Culture," *Developmental Brain Research*, 21:257-264 (1985).

Anchan et al., "Trophic Factors Influence Proliferation of Germinal Neuroepithelial Cells of the Retina," *J. Cell Biol.*, 109:58a, Abstract No. 308 (1989).

Anchan et al., "EGF and TGF- $\alpha$  Stimulate Retinal Neuroepithelial Cell Proliferation in Vitro," *Neuron*, 6(6):923-936 (1991).

Bayer et al., "Neuron production in the Hippocampus and olfactory bulb of the adult rat Brain: addition or replacement?", *Annals NY Acad. Sci.* 457:163-172 (1985).

Björklund et al., "Neural Grafting in Animal Models of Neurodegenerative Diseases," *Ann. New York Acad. Sci.*, 457:53-81 (1985).

Bouvier et al., "Basic Fibroblast Growth Factor (bFGF) Promotes the Survival and Proliferation of Mesencephalic Neuronal Precursors in Vitro," *Society for Neuroscience Abstracts*, vol. 18, Abstract No.: 403.7 (1992).

Boyles et al., "Accumulation of Apolipoproteins in the Regenerating and Remyelinating Mammalian Peripheral Nerve," *J. Biol. Chem.*, 265(29):17805-17815 (1990).

Calof et al., "Analysis of Neurogenesis in a Mammalian Neuroepithelium: Proliferation and Differentiation of an Olfactory Neuron Precursor in Vitro," *Neuron*, 3:115-127 (1989).

Cattaneo et al., "Identifying and Manipulating neuronal stem cells," *TINS*, 14(8): 338-340 (1991).

Cattaneo et al., "Proliferation and differentiation of neuronal stem cells regulated by nerve growth factor," *Nature*, 347:762-765 (1990).

Cepko "Immortalization of neural cells via retrovirus-mediated oncogene transduction," *Ann. Rev. Neurosci.*, 12:47-65 (1989).

Deloulme et al., "Establishment of Pure Neuronal Cultures From Fetal Rat Spinal Cord and Proliferation of the Neuronal Precursor Cells in the Presence of Fibroblast Growth Factor," *Journal of Neuroscience Research*, 29:499-509 (1991).

Dunnnett et al., "Dopamine-rich transplants in experimental Parkinsonism," *TINS*, 266-270 (Jul. 1983).

Emerich et al., "Behavioral Effects of Neural Transplantation," *Cell Transplantation*, 1:1-27 (1992).

Faaland et al., "Rapid uptake of tyrphostin into A431 human epidermoid cells is followed by delayed inhibition of epidermal growth factor (EGF)-stimulated EGF receptor tyrosine kinase activity", *Mol. Cell Biol.* 11(5):2697-2703 (1991).

(List continued on next page.)

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[57]

## ABSTRACT

A method for the in vitro proliferation and differentiation of neural stem cells and stem cell progeny comprising the steps of (a) isolating the cells from a mammal, (b) exposing the cells to a culture medium containing a growth factor, (c) inducing the cells to proliferate, and (d) inducing the cells to differentiate is provided.